

WO 03/086445

PCT/US03/10489

What is claimed is:

1. A method for qualifying hepatocellular carcinoma status in a subject, comprised of analyzing a biological sample from said subject for a diagnostic level of a protein selected from a first group consisting of

(A) I-M1, I-M2, I-M3, I-M4, I-M5, I-M6, I-M7, I-M8, I-M9, I-M10, I-M11, I-M12, I-M13, I-M14, I-M15, I-M16, I-M17, I-M18, I-M19, I-M20, I-M21, I-M22, I-M23, I-M24, I-M25, I-M26, I-M27, I-M28, I-M29, I-M30, I-M31, I-M32, I-M33, I-M34, I-M35, I-M36, I-M37, I-M38, I-M39, I-M40, I-M41, I-M42, I-M43, I-M44, I-M45, I-M46, I-M47, I-M48, I-M49, I-M50, I-M51, I-M52, I-M53, I-M54, I-M55, I-M56, I-M57, I-M58, I-M59, I-M60, I-M61, I-M62, I-M63, I-M64, I-M65, I-M66, I-M67, I-M68, I-M69, I-M70, I-M71, I-M72, I-M73, I-M74, I-M75, I-M76, I-M77, I-M79, I-M80, I-M81, I-M82, I-M83, I-M84, I-M85, I-M86, I-M87, I-M88, I-M89, I-M90, I-M91, I-M92, I-M93, I-M94, I-M95, I-M96, I-M97, I-M98, I-M99, I-M100

and/or a second group consisting of

(B) W-M1, W-M2, W-M3, W-M4, W-M5, W-M6, W-M7, W-M8, W-M9, W-M10, W-M11, W-M12, W-M13, W-M14, W-M15, W-M16, W-M17, W-M18, W-M19, W-M20, W-M21, W-M22, W-M23, W-M24, W-M25, W-M26, W-M27, W-M28, W-M29, W-M30, W-M31, W-M32, W-M33, W-M34, W-M35, W-M36, W-M37, W-M38, W-M39, W-M40, W-M41, W-M42, W-M43, W-M44, W-M45, W-M46, W-M47, W-M48, W-M49, W-M50, W-M51, W-M52, W-M53, W-M54, W-M55, W-M56, W-M57, W-M58, W-M59, W-M60, W-M61, W-M62, W-M63, W-M64, W-M65, W-M66, W-M67, W-M68, W-M69, W-M70, W-M71, W-M72, W-M73, W-M74, W-M75, W-M76, W-M77, W-M79, W-M80, W-M81, W-M82, W-M83, W-M84, W-M85, W-M86, W-M87, W-M88, W-M89, W-M90, W-M91, W-M92, W-M93, W-M94, W-M95, W-M96, W-M97, W-M98, W-M99, W-M100,

WO 03/086445

PCT/US03/10489

wherein said level is elevated relative to a norm.

2. A method for qualifying hepatocellular carcinoma status in a patient according to claim 1, wherein said protein is selected from the group consisting of

(A) I-M1, I-M3, I-M4, I-M5, I-M6, I-M7, I-M9, I-M11, I-M12, I-M13, I-M18, I-M19, I-M20, I-M21, I-M22, I-M23, I-M25, I-M26, I-M28, I-M32, I-M34, I-M36, I-M37, I-M41, I-M44, I-M46, I-M47, I-M52, I-M53, I-M64, I-M68, I-M69, I-M77, I-M79, I-M81, I-M84, I-M87, I-M88, I-M89, and I-M92

and/or a second group consisting of

(B) W-M1, W-M2, W-M3, W-M4, W-M5, W-M7, W-M9, W-M10, W-M11, W-M12, W-M13, W-M14, W-M15, W-M16, W-M17, W-M18, W-M19, W-M20, W-M21, W-M22, W-M23, W-M25, W-M26, W-M27, W-M30, W-M31, W-M33, W-M34, W-M35, W-M36, W-M39, W-M40, W-M41, W-M43, W-M44, W-M46, W-M47, W-M48, W-M49, W-M50, W-M52, W-M53, W-M54, W-M55, W-M58, W-M60, W-M62, W-M63, W-M70, W-M71, W-M73, W-M76, W-M78, W-M84, W-M86, W-M88, W-M89, W-M90, W-M93, W-M95, W-M96, W-M98, and W-M100.

3. A method according to claim 2, wherein said protein is I-M13, I-M18, I-M19, W-M2, or W-M23.

4. A method for qualifying hepatocellular carcinoma risk in a patient, comprising

(A) providing a spectrum generated by mass spectroscopic analysis of a biological sample taken from the subject, and

WO 03/086445

PCT/US03/10489

(B) extracting data from the spectrum and subjecting the data to pattern-recognition analysis that is keyed to at least one peak selected from

a first group consisting of

- (i) I-M1, I-M3, I-M4, I-M5, I-M6, I-M7, I-M9, I-M11, I-M12, I-M13, I-M18, I-M19, I-M20, I-M21, I-M22, I-M23, I-M25, I-M26, I-M28, I-M32, I-M34, I-M36, I-M37, I-M41, I-M44, I-M46, I-M47, I-M52, I-M53, I-M64, I-M68, I-M69, I-M77, I-M79, I-M81, I-M84, I-M87, I-M88, I-M89, and I-M92,

and/or a second group consisting of

- (ii) W-M1, W-M2, W-M3, W-M4, W-M5, W-M7, W-M9, W-M10, W-M11, W-M12, W-M13, W-M14, W-M15, W-M16, W-M17, W-M18, W-M19, W-M20, W-M21, W-M22, W-M23, W-M25, W-M26, W-M27, W-M30, W-M31, W-M33, W-M34, W-M35, W-M36, W-M39, W-M40, W-M41, W-M43, W-M44, W-M46, W-M47, W-M48, W-M49, W-M50, W-M52, W-M53, W-M54, W-M55, W-M58, W-M60, W-M62, W-M63, W-M70, W-M71, W-M73, W-M76, W-M78, W-M84, W-M86, W-M88, W-M89, W-M90, W-M93, W-M95, W-M96, W-M98, and W-M100.

5. A method according to claim 4, wherein said pattern-recognition analysis is keyed to a pair of peaks selected from

(A) I-M13 and I-M25, I-M13 and I-M7, I-M25 and I-M46, I-M37 and I-M77, I-M5 and I-M36, and/or

WO 03/086445

PCT/US03/10489

(B) W-M14 and W-M98, W-M21 and W-M46, W-M11 and W-M52, W-M16 and W-M89, W-M1 and W-M46, W-M21 and W-M76, W-M11 and W-M33, W-M13 and W-M18, W-M2 and W-M46, W-M33 and W-M54, W-M2 and W-M46, W-M16 and W-M46, W-M11 and W-M5.

6. A method according to claim 4, wherein said pattern-recognition analysis is keyed to a triplet of peaks selected from

(A) I-M1, I-M4 and I-M36; I-M5, I-M7 and I-M19; I-M7, I-M19 and I-M46; I-M9, I-M34 and I-M52; I-M7, I-M18 and I-M47; I-M11, I-M13 and I-M36; I-M9, I-M77 and I-M84; and I-M18, I-M22 and I-M79, and/or

(B) W-M21, W-M22 and W-M35; W-M7, W-M21 and W-M46; W-M13, W-M14 and W-M98; W-M14, W-M54 and W-M70; W-M11, W-M33 and W-M46; W-M17, W-M36 and W-M98; W-M19, W-M21 and W-M22; W-M14, W-M15, W-M54; W-M55, W-M58 and W-M98; W-M11, W-M14 and W-M98; W-M1, W-M33 and W-M46; W-M40, W-M46 and W-M49; W-M15, W-M21 and W-M22; W-M14, W-M36 and W-M98; W-M5, W-M11 and W-M54; W-M14, W-M22 and W-M25; W-M14, W-M58 and W-M98; W-M5, W-M14 and W-M89; W-M7, W-M14 and W-M89; W-M14, W-M21 and W-M98; W-M11, W-M58 and W-M71; W-M14, W-M25 and W-M54; W-M14, W-M60 and W-M89; W-M21, W-M46 and W-M100.

7. A method according to claim 4, wherein said pattern-recognition analysis is keyed to a combination of peaks selected from

(A) I-M11, I-M13, I-M19 and I-M89; I-M13, I-M19, I-M22 and I-M26; I-M1, I-M5, I-M36 and I-M41; I-M19, I-M33, I-M44 and I-M46; I-M3, I-M18, I-M68 and I-M81; I-M3, I-M12, I-M34 and I-M81; I-M12, I-M13, I-M32 and I-M37; I-M18, I-M44, I-M46 and I-M79; I-M7, I-M13, I-M21 and I-M23; I-M3, I-M18, I-M77 and I-M92; I-M12, I-M13, I-M77

WO 03/086445

PCT/US03/10489

and I-M87; I-M6, I-M13, I-M34 and I-M81; I-M8, I-M19, I-M53, I-M64, I-M69; I-M4, I-M18, I-M28, I-M47 and I-M88; and I-M1, I-M4, I-M18, I-M36, I-M41 and I-M47, and/or

(B) W-M25, W-M55, W-M62 and W-M98; W-M7, W-M14, W-M17 and W-M89; W-M17, W-M31, W-M93 and W-M98; W-M11, W-M19, W-M46 and W-M50; W-M4, W-M33, W-M55 and W-M98; W-M5, W-M11, W-M36 and W-M54; W-M16, W-M36, W-M43 and W-M46; W-M11, W-M41, W-M54 and W-M73; W-M5, W-M11, W-M52 and W-M89; W-M4, W-M14, 58 and W-M89; W-M2, W-M12, W-M14, W-M89; W-M5, W-M11, W-M20 and W-M40; W-M21, W-M46, W-M70 and W-M88; W-M21, W-M33, W-M34 and W-M46; W-M17, W-M20, W-M40 and W-M58; W-M17, W-M33, W-M52 and W-M98; W-M3, W-M7, W-M21 and W-M46; W-M10, W-M22, W-M30 and W-M95; W-M1, W-M46, W-M54 and W-M70; W-M11, W-M14, W-M25 and W-M54; W-M11, W-M33, W-M46 and W-M90; W-M11, W-M14, W-M54 and W-M89; W-M7, W-M18, W-M21 and W-M22; W-M17, W-M20, W-M52 and W-M98; W-M2, W-M15, W-M19, W-M22 and W-M55; W-M17, W-M19, W-M26, W-M47 and W-M98; W-M9, W-M11, W-M27, W-M46 and W-M78; W-M5, W-M11, W-M33, W-M46 and W-M53; W-M2, W-M9, W-M15, W-M19 and W-M89; W-M5, W-M11, W-M52, W-M89 and W-M96; W-M16, W-M25, W-M40, W-M52 and W-M89; W-M14, W-M15, W-M21, W-M22 and W-M89; W-M5, W-M13, W-M16, W-M20 and W-M98; W-M9, W-M23, W-M26, W-M40 and W-M89; W-M20, W-M27, W-M30, W-M35, W-M40 and W-M70; W-M13, W-M26, W-M39, W-M44, W-M63 and W-M98; W-M5, W-M13, W-M35, W-M39, W-M86 and W-M89; and W-M3, W-M18, W-M21, W-M22, W-M48, and W-M84.

WO 03/086445

PCT/US03/10489

8. A kit for detecting and diagnosing hepatocellular carcinoma, comprising

(A) an adsorbent attached to a substrate that retains one or more of the biomarkers selected from either a first group consisting of

(i) I-M1, I-M2, I-M3, I-M4, I-M5, I-M6, I-M7, I-M8, I-M9, I-M10, I-M11, I-M12, I-M13, I-M14, I-M15, I-M16, I-M17, I-M18, I-M19, I-M20, I-M21, I-M22, I-M23, I-M24, I-M25, I-M26, I-M27, I-M28, I-M29, I-M30, I-M31, I-M32, I-M33, I-M34, I-M35, I-M36, I-M37, I-M38, I-M39, I-M40, I-M41, I-M42, I-M43, I-M44, I-M45, I-M46, I-M47, I-M48, I-M49, I-M50, I-M51, I-M52, I-M53, I-M54, I-M55, I-M56, I-M57, I-M58, I-M59, I-M60, I-M61, I-M61, I-M62, I-M63, I-M64, I-M65, I-M66, I-M67, I-M68, I-M69, I-M70, I-M71, I-M72, I-M73, I-M74, I-M75, I-M76, I-M77, I-M79, I-M80, I-M81, I-M82, I-M83, I-M84, I-M85, I-M86, I-M87, I-M88, I-M89, I-M90, I-M91, I-M92, I-M93, I-M94, I-M95, I-M96, I-M97, I-M98, I-M99, I-M100

or a second group consisting of

(ii) W-M1, W-M2, W-M3, W-M4, W-M5, W-M6, W-M7, W-M8, W-M9, W-M10, W-M11, W-M12, W-M13, W-M14, W-M15, W-M16, W-M17, W-M18, W-M19, W-M20, W-M21, W-M22, W-M23, W-M24, W-M25, W-M26, W-M27, W-M28, W-M29, W-M30, W-M31, W-M32, W-M33, W-M34, W-M35, W-M36, W-M37, W-M38, W-M39, W-M40, W-M41, W-M42, W-M43, W-M44, W-M45, W-M46, W-M47, W-M48, W-M49, W-M50, W-M51, W-M52, W-M53, W-M54, W-M55, W-M56, W-M57, W-M58, W-M59, W-M60, W-M61, W-M61, W-M62, W-M63, W-M64, W-M65, W-M66, W-M67, W-M68, W-M69, W-M70, W-M71, W-M72, W-M73, W-M74, W-M75, W-M76, W-M77, W-M79, W-M80, W-M81, W-M82, W-M83, W-M84, W-M85, W-M86, W-M87, W-M88,

WO 03/086445

PCT/US03/10489

W-M89, W-M90, W-M91, W-M92, W-M93, W-M94, W-M95, W-M96,
W-M97, W-M98, W-M99, W-M100,

(B) instructions to detect the biomarker(s) by contacting a sample with the adsorbent and detecting the biomarker(s) retained by the adsorbent.

9. A kit according to claim 8, further comprising a washing solution or instructions for making a washing solution.

10. A kit according to claim 8, wherein the substrate is a SELDI probe that comprises either (i) functionalities that adsorb transition metal ions by chelation or (ii) functionalities that allow for cation exchange.

11. Software for qualifying hepatocellular carcinoma status in a subject, comprising an algorithm for analyzing data extracted from a spectrum generated by mass spectroscopic analysis of a biological sample taken from the subject, wherein said data relates to one or more biomarkers selected from either a first group consisting of

(i) I-M1, I-M2, I-M3, I-M4, I-M5, I-M6, I-M7, I-M8, I-M9, I-M10, I-M11, I-M12, I-M13, I-M14, I-M15, I-M16, I-M17, I-M18, I-M19, I-M20, I-M21, I-M22, I-M23, I-M24, I-M25, I-M26, I-M27, I-M28, I-M29, I-M30, I-M31, I-M32, I-M33, I-M34, I-M35, I-M36, I-M37, I-M38, I-M39, I-M40, I-M41, I-M42, I-M43, I-M44, I-M45, I-M46, I-M47, I-M48, I-M49, I-M50, I-M51, I-M52, I-M53, I-M54, I-M55, I-M56, I-M57, I-M58, I-M59, I-M60, I-M61, I-M61, I-M62, I-M63, I-M64, I-M65, I-M66, I-M67, I-M68, I-M69, I-M70, I-M71, I-M72, I-M73, I-M74, I-M75, I-M76, I-M77, I-M79, I-M80, I-M81, I-M82, I-M83, I-M84, I-M85, I-M86, I-M87, I-M88, I-M89, I-M90, I-M91, I-M92, I-M93, I-M94, I-M95, I-M96, I-M97, I-M98, I-M99, I-M100

or a second group consisting of

WO 03/086445

PCT/US03/10489

(ii) W-M1, W-M2, W-M3, W-M4, W-M5, W-M6, W-M7, W-M8, W-M9, W-M10, W-M11, W-M12, W-M13, W-M14, W-M15, W-M16, W-M17, W-M18, W-M19, W-M20, W-M21, W-M22, W-M23, W-M24, W-M25, W-M26, W-M27, W-M28, W-M29, W-M30, W-M31, W-M32, W-M33, W-M34, W-M35, W-M36, W-M37, W-M38, W-M39, W-M40, W-M41, W-M42, W-M43, W-M44, W-M45, W-M46, W-M47, W-M48, W-M49, W-M50, W-M51, W-M52, W-M53, W-M54, W-M55, W-M56, W-M57, W-M58, W-M59, W-M60, W-M61, W-M61, W-M62, W-M63, W-M64, W-M65, W-M66, W-M67, W-M68, W-M69, W-M70, W-M71, W-M72, W-M73, W-M74, W-M75, W-M76, W-M77, W-M79, W-M80, W-M81, W-M82, W-M83, W-M84, W-M85, W-M86, W-M87, W-M88, W-M89, W-M90, W-M91, W-M92, W-M93, W-M94, W-M95, W-M96, W-M97, W-M98, W-M99, W-M100,

12. Software according to claim 11, wherein said algorithm carries out a pattern-recognition analysis that is keyed to data relating to at least one of the biomarkers.

13. Software according to claim 12, wherein said algorithm comprises classification tree analysis that is keyed to data relating to at least one of the biomarkers.

14. Software according to claim 12, wherein said algorithm comprises artificial neural network analysis that is keyed to data relating to at least one of the biomarkers